

## Less Commonly Recognized Clinical Features of Amebiasis

MERVIN J. GOLDMAN, M.D., *Oakland*

### SUMMARY

*Among the less commonly recognized clinical manifestations of intestinal and hepatic amebiasis are vague abdominal distress in the absence of diarrhea, symptoms like those of peptic ulcer, and symptoms of a kind that may be ascribed to psychoneurosis. Hepatic amebiasis may be confused with other diseases affecting areas above or below the right diaphragm, such as cholecystitis, viral hepatitis, pneumonia or pleurisy.*

*Adequate therapy in every case must include a course of a drug effective against hepatic involvement (chloroquine or emetine) and a drug effective against intestinal involvement (Diodoquin, Milibis, or carbarsone). Even in the absence of positive results of stool examinations, a course of antiamebic therapy is always justified as a diagnostic and therapeutic measure.*

REPORTS of experience during and after World War II have made physicians in general aware that amebiasis is not exclusively a tropical disease, and most of them consider the disease when a patient complains of diarrhea, particularly if the diarrhea is acute, with discharge of blood. However, since the diagnosis may be missed (or erroneous diagnosis made) if diarrhea is not present to arouse suspicion, awareness of other, less forthright manifestations of amebiasis is important.

The occurrence of diarrhea is by no means a requirement for the diagnosis of amebiasis. Indeed, in chronic amebiasis the bowel movements may be entirely normal, or constipation may be present. It is noteworthy, moreover, that diarrhea may not be recognized as such by a patient unless it is severe. Close questioning is necessary, for to most laymen the word means frequent watery bowel movements. The more characteristic pattern of chronic intestinal amebiasis is the passage of one or more "mushy" stools a day. Not infrequently a war veteran denies having diarrhea, only to admit on further questioning that he passed one normally formed stool a day before military service and one mushy stool daily afterward.

Vague symptoms referable to the gastrointestinal tract, such as indigestion or indefinite abdominal

pains, with or without abnormally formed stools, may result from intestinal amebiasis. Not infrequently in cases in which such symptoms are ascribed to psychoneurosis after extensive x-ray studies have been carried out, complete relief is obtained with antiamebic therapy.

Sometimes associated with amebiasis are symptoms like those of peptic ulcer but with no abnormality observable in x-ray studies. Then, after *E. histolytica* is noted in the stool and antiamebic therapy given, the symptoms of ulcer disappear. The reason for gastric distress as a concomitant of amebiasis is not clear; the phenomenon may be caused by reflex pylorospasm secondary to the colonic involvement.

Differentiating between acute amebiasis and acute appendicitis may be exceedingly difficult. In 85 per cent of cases of amebiasis, the cecum is involved.<sup>4</sup> Amebiasis of the appendix likewise occurs. In some instances, even the observation of *E. histolytica* in the stool may not rule out appendicitis and the clinical symptoms may be such as to dictate surgical intervention. In such circumstances it is imperative that emetine be given preoperatively. Even if amebiasis is not diagnosed preoperatively, if the surgeon upon opening the abdomen becomes suspicious of amebiasis from examination of the appendix or colon, emetine should be given immediately. Beginning treatment at this stage will prevent or greatly minimize the danger of amebic peritonitis, which often causes death.

Chronic amebiasis may simulate non-specific ulcerative colitis. Furthermore, non-specific ulcerative colitis may follow amebic colitis, in which case eradication of the amebae with proper therapy will not bring about a cure. Although lesions of the two diseases, viewed sigmoidoscopically, usually are distinctive, this is not always the case. It is therefore advisable that every patient with chronic colitis be given antiamebic therapy even though the organisms are not observed in repeated examinations of stools. A brief report of a case will illustrate:

A young woman was examined at an excellent university medical center because of chronic diarrhea. Conditions observed in a sigmoidoscopic examination were consistent with chronic non-specific ulcerative colitis. Repeated stool examinations were negative for ova and parasites. The patient was told she had chronic ulcerative colitis and was discharged. The symptoms persisted and one year later the patient entered another hospital, received a course of antiamebic treatment and was immediately and completely relieved of symptoms. There was no recurrence in a two-year follow-up period.

In some instances following antiamebic therapy, residual symptoms such as mild pain and some frequency of bowel movement continue. Often in such circumstances the patient is overtreated with re-

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peated courses of amebicides and medicated enemas without clinical improvement. It seems logical that residual inflammatory changes (or additional disease such as a bacterial dysentery requiring other therapy) may be present, even after the amebae have been eliminated, and that they cause the symptoms mentioned. Treatment with diet and antispasmodics is indicated.

Allergic manifestations are not commonly mentioned. Eosinophilia is not a feature of amebiasis, and when it does occur is rarely over 15 per cent. In routine physical examination of soldiers with acute amebiasis it was not uncommon to note scattered rhonchi through both lung fields. This occurred in the absence of acute respiratory infection or history of asthma. Rarely was the patient aware of the condition and it abated during antiamebic therapy. In some instances patients who had repeated episodes of angioneurotic edema were not permanently relieved of the symptoms until incidental amebic infestation was diagnosed and treated. Although the foregoing were purely clinical observations, the conditions occurred frequently enough to seem significant.

#### SIGMOIDOSCOPIC EXAMINATION

In sigmoidoscopic inspection, if amebic disease is present in the rectosigmoid region ulcers of varying size can be seen, with fairly normal mucous membrane between the areas of ulceration. This is in contrast to the usual appearance in non-specific ulcerative colitis wherein the entire mucous membrane is granular, friable and abnormal. However, this differential point is not absolute.

When lesions are noted it is essential to obtain material for microscopic examination. It is practically useless to attempt to get a proper specimen with a cotton swab. Use of an instrument with a dull small curette at the end is advisable, so that the ulcer may be gently scraped and all the material obtained saved for immediate examination.

Amebiasis may be present even though the rectosigmoid region appears to be entirely normal, since the lesions may be elsewhere in the colon.

#### STOOL EXAMINATIONS

For the highest degree of accuracy in examination of stools, the specimens must be collected properly and examined by well trained and experienced technicians. In examination for the trophozoites, freshly passed stools are essential. Administration of a saline laxative with immediate examination of the resulting diarrheal stools sometimes facilitates diagnosis. Specimens of formed stools are satisfactory for use in search for cysts, but the diagnosis should not be made on the basis of an unstained preparation alone. It is always wise to verify suspicious cysts with an iron-hematoxylin stain. With the development of good preservative material it is now possible to send specimens by mail to laboratories which are equipped to carry out these procedures.

Since the finding of the amebae can be so difficult, no examination should be considered complete until six to nine specimens have been examined.

#### COMPLICATIONS

*Intestinal.* Severe bleeding and perforation are very rare complications of intestinal amebiasis. Chronic ulcerative colitis and the "irritable colon" syndrome were previously discussed.

*Hepatic.* This is the most common complication. On routine physical examination of soldiers with acute amebiasis, in about 20 per cent of cases enlargement and tenderness of the liver were noted. The condition abated when antiamebic therapy was carried out.

Sixty to 90 per cent of patients with hepatic amebiasis have a history of diarrhea. In 60 to 75 per cent of cases the organism is noted in the stools. Therefore, neither the absence of a history of diarrhea nor the absence of *E. histolytica* in the stools excludes the diagnosis. The term "hepatitis" is actually a misnomer since there is not a diffuse inflammatory process throughout the liver, but localized areas of involvement. Likewise the term "abscess" is incorrect inasmuch as the involved area, unless secondarily infected, does not contain pus, but merely necrotic and autolyzed liver tissue.

The characteristic clinical features are chills, fever, and pain and tenderness in the right upper quadrant of the abdomen and in the lower part of the chest on the right side. Frequently observed in fluoroscopic examination of the chest are elevation, deformity and splinting of the right diaphragm. Jaundice other than of a very mild degree is rare. From this typical form there are all gradations to entirely asymptomatic cases. In epidemic areas hepatic lesions not infrequently are noted at autopsy in cases in which there was no clinical evidence of disease of the liver. The disease may be manifest in morbid process above the diaphragm on the right side. One such case was that of a soldier who was admitted to an overseas general hospital after an illness of one week characterized by chills, fever and pain low in the chest on the right side. Upon examination pleural effusion on the right side was noted, and aspirated material contained many lymphocytes. Low grade fever continued and the diagnosis was tuberculous pleural effusion until the patient's field medical records arrived and it was noted in them that earlier the liver had been palpable and tender. *E. histolytica* then were observed in the stool. Antiamebic therapy resulted in immediate disappearance of all signs and symptoms.

Another patient who had been hospitalized for dental extractions at another excellent medical installation was transferred for treatment of "arthritis" of the right shoulder. Careful questioning and examination elicited that pain in the right shoulder was referred from the right side of the diaphragm, which was elevated and splinted. *E. histolytica* were present in the stools. Following antiamebic therapy the "arthritis" abated.

Differentiating between acute gallbladder disease and acute hepatic amebiasis may be exceedingly difficult. X-ray studies of the gallbladder and a diagnostic trial of antiamebic therapy may be nec-

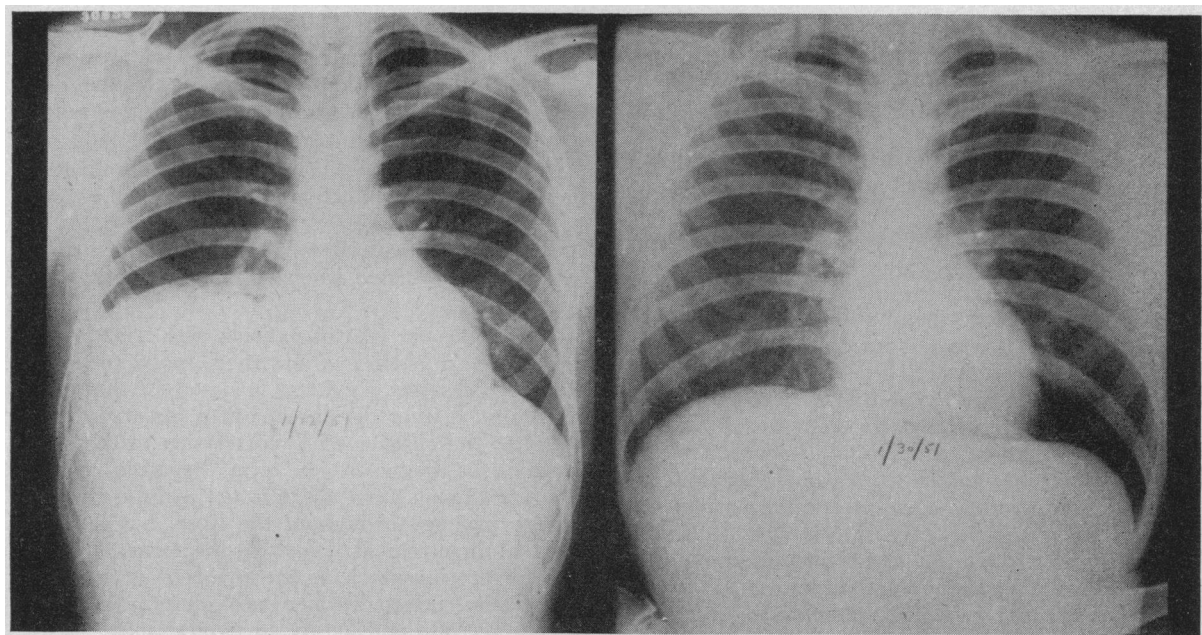


Figure 1.—*Left*—Chest roentgenogram taken before treatment. *Right*—18 days later: return of right diaphragm to normal position with clearing of the neighborhood reaction at the right lung base.

essary to differentiate the two conditions. To illustrate: A 25-year-old male was admitted to hospital with complaints of chills, fever, and pain in the right upper quadrant of the abdomen. There was pronounced tenderness in the painful quadrant of the abdomen and in the rib cage low on the right side. The patient gave a history of diarrhea while serving in the armed forces. *E. histolytica* were observed in the stools. Antiamoebic treatment was carried out and all symptoms disappeared within a few days. X-ray studies of the gallbladder were not done. The patient returned several months later with identical complaints. The gallbladder could not be visualized by x-ray and the diagnosis of cholecystitis and cholelithiasis was proved at operation.

An amoebic liver "abscess" may rupture spontaneously. Fortunately, in most cases rupture is into a bronchus, but rupture into any neighboring body cavity or organ may occur.

#### TREATMENT

Since hepatic involvement is common in amebiasis and since this feature may not be clinically apparent, it is essential that each patient be treated with drugs which will eradicate both the intestinal and the hepatic foci.

**Emetine.** Until recently emetine was the only drug which was of value in the treatment of hepatic amebiasis. The dangers of this drug have been tremendously exaggerated. However, to minimize the possible toxic effects of this drug it is necessary to keep the patient at rest in bed. In recent years chloroquine has been shown to be very efficacious in liver disease and since this drug is practically non-toxic and does not require restriction of the patient's activity, it is now the drug of choice. Thus emetine is limited to use, preoperatively and postoperatively,

in cases in which the patient cannot take medication orally, and in the rare cases of amoebic granuloma of another site. The usual dose of emetine is 0.065 gm. parenterally each day for six to ten days depending on the size of the patient and the severity of the disease. In cases of definite amoebic "abscess" of the liver, it will usually be necessary to give a second course of emetine (if chloroquine is not used) after a short rest period. While this therapy is being given, the patient is kept at rest and carefully observed as to blood pressure, pulse rate and evidence of peripheral nerve involvement. Some change may be noted in electrocardiograms, but this will rarely be of significance in the absence of clinical evidence of toxicity when the drug is used as outlined above.

**Chloroquine.** The effectiveness of this drug in hepatic amebiasis is based on its extensive localization in the liver<sup>2</sup> (some 500 times its plasma concentration). The usual dosage is 0.5 gm. twice daily for three days following 0.25 gm. twice daily for a total of two weeks. (See Figures 1 and 2.)

**Intestinal drugs.** Since neither emetine nor chloroquine is highly effective in the treatment of intestinal amebiasis, it is imperative that other medications which will eradicate the primary intestinal focus be given. The effective drugs in this group are the iodo-hydroxyquinolines (Diodoquin,<sup>®</sup> vioform and chiniofon), carbarsone and Milibis.<sup>®</sup> The author's experience has been mainly with Diodoquin and it has been found to be an exceedingly efficacious drug with practically no toxicity. The usual dose of Diodoquin is three tablets (0.63 gm.) three times daily for three weeks.

**Antibiotics.** In recent years there have been some favorable reports on the use of aureomycin in the

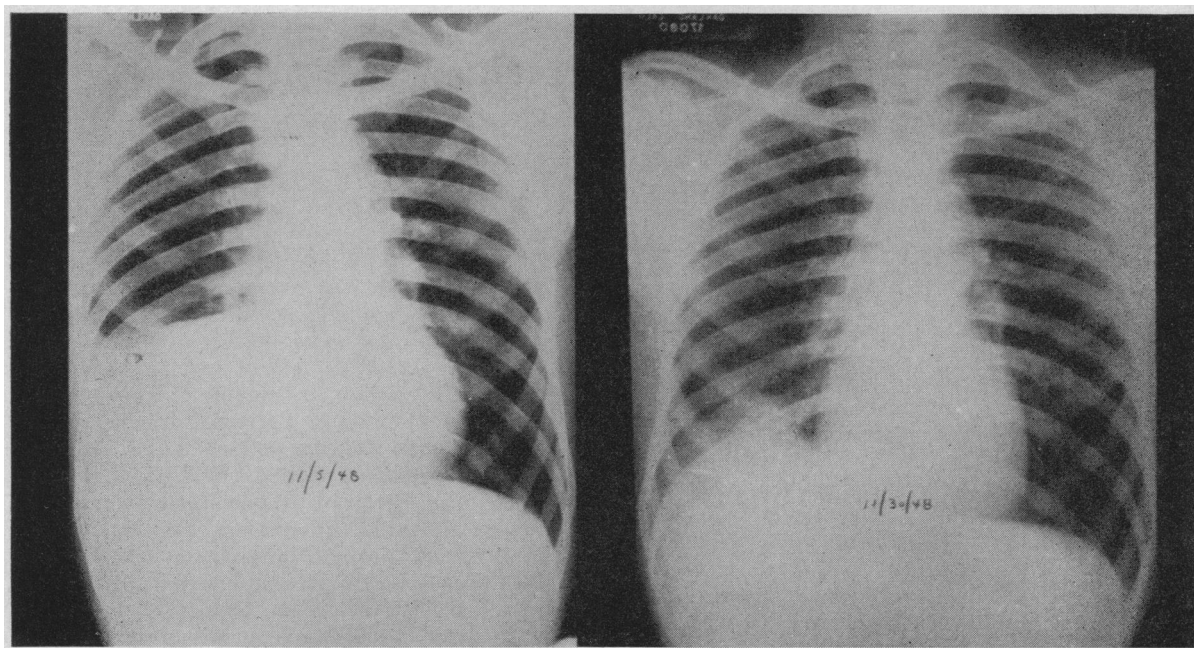


Figure 2.—*Left*—Roentgenogram before therapy in which it was noted that right diaphragm was elevated and splinted, with some reaction at the base of the right lung. *Right*—25 days later: considerable improvement but not complete return to normal.

treatment of amebiasis. However, experimental studies on monkeys<sup>1</sup> and one recent clinical report in the treatment of 25 patients,<sup>3</sup> very strongly question the value of this drug as an amebicide. Until there is further evidence in its favor and since more certain drugs are available, aureomycin should not be relied upon as the sole agent in the treatment of amebiasis.

Thus, from the standpoint of effectiveness, lack of toxicity and lack of necessity for restricting the activity of the patient, a course of chloroquine for two weeks and a course of Diodoquin for three weeks (or one of the other effective intestinal drugs) is the treatment of choice in amebiasis.

*Drainage of liver "abscess."* In many instances of long standing and large amebic "abscesses," conservative treatment alone will not cure the patient. Removal of the necrotic material becomes necessary. The method of choice is closed needle aspiration, with local anesthesia. The site for puncture is the most tender point in the right intercostal spaces,

which will usually be the eighth or ninth right intercostal space in the anterior or mid-axillary line. In all instances, unless aspiration seems imperative as an emergency procedure, it should not be done until the patient has received chloroquine or emetine for several days to prevent the spread of amebae into the pleura or peritoneum. Open surgical drainage results in a tremendously higher mortality rate and should be used only if there are secondarily infected abscesses which do not respond to antiamebic therapy, antibiotics and closed aspiration.

Veterans Administration Hospital, 13th and Harrison Streets.

#### REFERENCES

1. Anderson, H., and Anderson, J.: Antibiotics against amebiasis in Macaques, *Am. J. Trop. Med.*, 30:193, Dec. 1950.
2. Conan, N. J.: The treatment of hepatic amebiasis with chloroquine, *Am. J. Med.*, 6:309-320, March 1949.
3. McHardy, G.: Aureomycin in the treatment of amebiasis, *Gastroenterology*, 17:113, Jan. 1951.
4. Napier, L. E.: *The Principles and Practice of Tropical Medicine*, The Macmillan Co., 1946.